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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,526	02/13/2001	Hiroshi Susaki	P20257	3623

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,526	SUSAKI ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *21* is/are allowed.

6)☒ Claim(s) *1,3-5,9-20 and 22* is/are rejected.

7)☒ Claim(s) *2 and 6-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Sequence Listing filed July 8, 2002 is approved.

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The abstract of the disclosure is objected to because of the presence of legal phraseology ("said"). Correction is required. See MPEP § 608.01(b).

4. The disclosure is objected to because of the following informalities: SEQ ID NOS must be inserted after those amino acid sequences in the specification (see, e.g., pages 16, 18-21, 26, 27, 29, and 30) which are subject to the sequence disclosure rules. See 37 CFR 1.821(d). Appropriate correction is required.

5. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There is no antecedent basis in the claims for the phrase "the drug compound having an amino group" at claim 10, lines 1-2. Note that independent claim 1, upon which claim 10 depends, does not require the drug compound to have an amino group. It is suggested that the phrase could be re-written as, e.g., "the drug compound has an amino group and".

6. Claims 12, 13, 16, 17, 19, and 20 are objected to because of the following informalities: SEQ ID NOS must be inserted after those amino acid sequences in the claims which are subject to the sequence disclosure rules. See 37 CFR 1.821(d). Appropriate correction is required.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 34 of copending Application No. 09/807,980. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim of the '980 application anticipates the instant claims. A method of using a product anticipates a claim drawn to the product.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

9. Claims 1, 3-5, 9, 10, 14, 18, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by the European Patent Application 624,377. The European Patent Application '377 teaches a conjugates in which a ligand L is conjugated through a carboxylic acyl unit A, one or more amino acids Y and Z, and one or two self-immolative spacers X and W, to a drug D. See Formula (I) at page 3, lines 35-54. The self-immolative spacer can have a structure of formula (III) (see page 5, lines 5-20), which corresponds to Applicants' NH-Y-CH_2-O-CO group. After enzymatic cleavage of the peptide, the self-immolative spacer spontaneously cleaves from the drug, releasing the drug in pharmacologically active form (see, e.g., page 4, line 46 - page 5, line 3). Preferred drugs includes those used for cancer therapy (see, e.g., page 9, lines 39-50), and the drugs can be linked to the self-immolative spacer via an amino group present in the drug (see, e.g., compound 9 at page 27; compound 15 at page 29; and compound 24 at page 31). The

ligands can be antibodies or fragments thereof, proteins, and polypeptides (see, e.g., page 19, line 3 - page 23, line 37), which are polymers. A final product is exemplified in Example 81. The European Patent Application '377 also teaches intermediates, e.g., compound 9 at page 27; compound 15 at page 29; and compound 24 at page 31; which comprise the spacer linked to the drug prior to reaction with the ligand, and which has the same structure as in Applicants' claim 18. With respect to claim 22, an intended use limitation does not impart patentability to product claims where the product is otherwise anticipated by the prior art.

The rejection of claims 1, 3-5, 9, 10, and 14 assumes that the drug complex formula recited in instant claim 1 does not exclude the presence of the carboxylic acyl unit A which is required to be present by the European Patent Application '377, or assumes that the carboxylic acyl unit A which is required to be present by the European Patent Application '377 can be considered to form part of the polymer A as recited in the drug complex formula of instant claim 1. Applicants may wish to address this issue in their response to this Office action.

10. Claims 11 and 15 are rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 624,377 as applied against claims 1, 3-5, 9, 10, 14, 18, and 22 above, and further in view of the Japanese Patent Application 06-87746. The European Patent Application '377 teaches the use of anti-cancer agents in general, but does not teach conjugates in which the drug has the structure specified in instant claims 11 and 15. The Japanese Patent Application '746 teaches the drug of Applicants' claims 11 and 15 to be a useful antitumor agent having activity against a variety of cancers. See, e.g., the Abstract. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the antitumor agents of the Japanese Patent Application '746 to form the conjugates of the European Patent

Application '377 because the antitumor agents of the Japanese Patent Application '746 are generically embraced by the European Patent Application '377 and because conjugation of the specific antitumor agents of the Japanese Patent Application '746 in accordance with the European Patent Application '377 would have been expected to result in a conjugate product with activity against a wide variety of cancers.

11. Claims 12, 13, 16, 17, 19, and 20 are rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 624,377 in view of the Japanese Patent Application 06/87746 as applied against claims 11 and 15 above, and further in view of the WO Patent Application 97/46260. (The examiner relies upon the European Patent Application 0 916 348 as a translation of the WO Patent Application '260. All citations in the rejection will use the page, line, and claim numbers of the European Patent Application '348). The European Patent Application '377 does not teach a peptide portion of the conjugate having the sequences Gly-Gly-Phe-Gly or Gly-Gly-Gly-Phe. The WO Patent Application '260 teaches conjugates comprising a carboxy(C_{1-4})alkyldextran polyalcohol linked through a peptide spacer to a drug which can be the same as the drug specified in Applicants' claims 11 and 15. The spacer can be chosen to achieve an optimum releasing rate for the drug, e.g., can be -Gly-Gly-Phe-Gly if a high releasing rate is desired and can be -Gly-Gly-Gly-Phe- if a relatively low releasing rate is desired. See, e.g., the Abstract; page 3, lines 27-28 and 38-49; page 6, lines 14-22; and page 7, Table 1. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use any of the spacers disclosed in the WO Patent Application '260, e.g., Gly-Gly-Phe-Gly or Gly-Gly-Gly-Phe, to form the peptide portion of the conjugates of the European Patent Application '377 as modified above by the Japanese Patent Application '746,

because the European Patent Application '377 is not limited to any particular peptide sequence, and because choosing from among the spacers taught by the WO Patent Application '260 permits one to achieve an optimum releasing rate for the drug.

12. Claims 18 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by D'Amico et al (U.S. Patent No. 6,368,598). D'Amico et al teach conjugates comprising a cleavable peptide linked to a good leaving group which corresponds to Applicants' NH-Y-CH_2-O-CO group, which is linked to an anti-cancer drug such as adriamycin. See, e.g., Figure 8; column 6, the structure at the bottom of the column; and claim 7, second structure. With respect to claim 22, an intended use limitation does not impart patentability to product claims where the product is otherwise anticipated by the prior art.

13. Claim 21 is allowed. Claims 2 and 6-8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

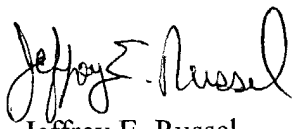
The European Patent Application 624,377 is not applied against instant claims 2 and 6-8 because the European Patent Application '377 requires a ligand that specifically binds or reactively associates or complexes with a receptor or other receptive moiety associated with a given target cell population. There is no suggestion in the prior art of record that the polysaccharide derivatives recited in instant claims 2 and 6-8 would exhibit this function required by the European Patent Application '377. The European Patent Application '377 is not applied against instant claim 21 because the disclosure of the European Patent Application '377 is limited to reacting the peptide-self-immolative spacer with the drug and then reacting the

ligand. The European Patent Application '377 does not provide any motivation to react the peptide-self-immolative spacer with the ligand prior to reacting it with the drug.

The WO Patent Application 98/19705 is cited as art of interest, being essentially duplicative of the European Patent Application '377 applied above. See, e.g., page 15, line 25 - page 16, line 3; page 17, lines 3-7; and page 44, compounds 21a-21b; of the WO Patent Application '705.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (571) 272-0961. The fax number for formal communications to be entered into the record is (703) 872-9306; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

April 1, 2004